REMARKS/ARGUMENTS

Claims 42-80 are currently pending in the application. Claims 52-56 and 65-74 have been withdrawn as being drawn to a non-elected invention. Claim 42 has been amended to incorporate the language of claim 47. The dependency of claims 50, 51 and 57 has been changed. Claim amendments are made without prejudice to filing a continuation or divisional application directed to the cancelled subject matter.

Elections/Restrictions

The Examiner has maintained that the restriction between the different target genes is proper because claim 42 is not currently an allowable linking claim. MPEP 809 states that where a restriction of the claims is proper but presented in the same case are one or more claims (generally called "linking" claims) which if allowable would require joinder of the otherwise divisible invention, the linking claims must be examined with, and thus are considered part of, the invention elected. Should any linking claim be allowable, the restriction requirement between the linked inventions must be withdrawn. Any claims directed to the nonelected invention previously withdrawn from consideration which depends from or requires all the limitations of the allowable linking claim must be rejoined and fully examined for patentability. Applicants maintain that claim 42 is a linking claim and rejoinder of claims 63-74 should be allowed upon allowance of claim 42.

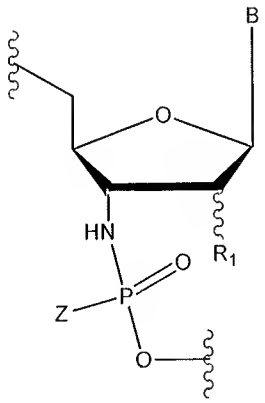
The Office indicates that it has required restriction between product and process claims. The Office has indicated that should a product claim subsequently be found to be allowable, withdrawn process claims that depend from or otherwise include all of the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right.

Claim Rejections under 35 U.S.C. §102

Claims 42-48, 50, 51, 57-64, and 75-80 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Manoharan et al. (US 2005/0164235). According to the Patent Office, Manoharan et al., allegedly teach iRNA molecules, including single or double-stranded siRNA molecules between 15-25 nucleobases in length comprising at least one or optionally all ribo-N3'-P5' phosphoramidate or thiophosphoramidate linkages, which iRNA has a lipid moiety covalently conjugated to its 5' or 3' terminus. The Office directs the applicant to pages 5, 6, 8-11, 22, 23, 35-37, 40, 42, 49, 53-54.

Applicant traverses this rejection on the following basis.

Applicant has amended claim 42 to rccite an isolated small interfering RNA (siRNA) comprising 15-25 nucleotides complementary to a target nucleic aeid sequence, wherein the RNA comprises at least one nucleotide of formula:



wherein R_1 is chosen from fluorine and OR_2, R_2 is chosen from hydrogen and lower alkyl, B is choscn from purines, pyrimidines, and analogs thereof, and Z is sulfur.

It is well settled that a prior genus which does not explicitly disclose a species does not anticipate a later claim to that species. *W.L. Gore & Associate v. Garlock Inc.* 842 F. 2d 1275, 6 USPQ 2d 1277 (Fed Cir 1983). This is especially the situation where the disclosed genus is very broad.

In Manoharan et al. (US 2005/0164235) a very large genus of RNAi compounds (in the thousands) is disclosed. Manoharan is primarily directed to an iRNA agent wherein at least one subunit has formula I or formula II incorporated into at least one of the strands. Formula I and formula II are specific saccharide moieties to optimize the properties of the iRNA agent. There are no species disclosed which have a N3→P5 thiophosphoramidate linkage. There is no teaching to direct one of skill in the art to make an iRNA compound having a N3→P5 thiophosphoramidate linkage. Absent such a showing, it is improper for the Patent Office to state that Manoharan anticipates the claimed genus.

Claims 42-44, 57, 59, 60, 61, and 78-80 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Davis (US2005/0136430). The Patent Office states that Davis allegedly teaches iRNA molecules, including simple or double-stranded siRNA molecules between 15-25 nucleobases in length comprising at least one or optionally all ribo N3→P5' thiophosphoramidate linkage. See esp. pages 3, 5-8, 14-16.

Applicant traverses this rejection on the following basis. There are no RNAi species disclosed which have a N3→P5 thiophosphoramidate linkage. There are no genus disclosed that includes a thiophosphoramidate linkage. There is no teaching to direct one of skill in the art to make an iRNA compound having a N3→P5 thiophosphoramidate linkage. There is no teaching of how to make such an iRNA. Absent such a showing, Davis does not anticipate the claimed invention. For these reasons, Applications request that the Patent Office withdraw these rejections.

Claim Rejections under 35 U.S.C. § 103

Claims 42-51, 57-64, 75-80 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Manoharan et al., and Davis et al., in combination in view of Jiang et al. (US2006/0116331).

Manoharan et al., (US2005/0164235) allegedly teach iRNA molecules, including single or double stranded siRNA molecules between 5-25 nucleobases in length comprising at least one N3→P5 thiophosphoramidate linkage, which iRNA has a lipid moiety conjugated to its 5' or 3'

terminus. Davis (US 2005/0136430) allegedly teach iRNA molecules including single or double stranded siRNA molecules between 15-25 nucleobases in length comprising at least one N3→P5 thiophosphoramidate linkage. The Office Action agrees that Manoharan and Davis do not teach fatty acids substituted with at least one fluorine. Jiang et al., (US 2006/0116331) allegedly teach oligonucleotides with covalently conjugated lipid moieties which lipids comprise fatty acids comprising at least one fluorine.

The Patent Office states that it allegedly would have been obvious to incorporate the fluorines into fatty acids or lipid groups that are covalently linked to inhibitory oligonucleotides because Jiang taught the method to do this and it was well known in the art that fluorocarbon group analogs have enhanced anti-HIV capabilities. One would allegedly be motivated to design these fluorine containing molecules and one would allegedly have a reasonable expectation lipophilicity of the oligonuclcotides would be enhanced.

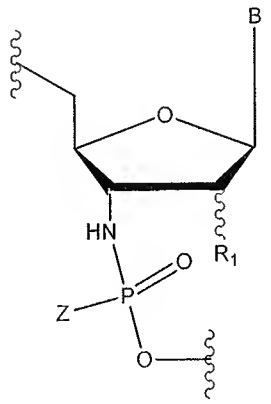
Applicants disagree for the following reasons. There is no teaching in Davis of oligonucleotides with N3→P5 thiophosphoramidate linkages. Manoharan discloses an extremely large genus of compounds but does not specifically teach oligonucleotides with N3→P5 thiophosphoramidate linkages. There is no motivation in Manoharan to choose from among the very large genus disclosed in Manoharan the very specific linkages to arrive at the N3→P5 thiophosphoramidate linkage of the present invention. Manoharan does not teach how to make such a linkage or any advantages of such a linkage relative to any other linkage. One would not be motivated to generate such a linkage, when Manoharan teaches how to generate other types of linkages. There is no teaching in Jiang et al. of oligonucleotides with covalently conjugated lipid moieties. Jiang is directed to glycosylceramide analogues. Jiang et al. does not teach the N3→P5 thiophosphoramidate linkage and accordingly does not cure this deficiency in Manoharan or in Davis. Absent a teaching of the claimed invention or a motivation to make such an invention, this rejection is improper. Applicants request that the rejection be withdrawn.

Claim Rejections under Obviousness Double Patenting

Claims 42-51, 57-64 and75-80 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of US Patent No. 7494982 in view of Gryaznov et al., (US 2005/0113325).

Applicant's note that Gryaznov et al., (US 2005/0113325) published after the PCT filing date of the present application. In addition, the inventive entity of Gryaznov et al., (US 2005/0113325) is the same as the present application. Accordingly, Gryaznov et al., (US 2005/0113325) is not prior art to the present application.

Secondly, Applicants note that the present application has been amended to claim small interfering RNA (siRNA) comprising 15-25 nucleotides complementary to a target nucleic acid sequence, wherein the RNA comprises at least one nucleotide of formula:



wherein R_1 is chosen from fluorine and OR_2, R_2 is chosen from hydrogen and lower alkyl, B is chosen from purines, pyrimidines, and analogs thereof, and Z is sulfur.

The claimed invention is not obvious in view of claims 1 and 2 of US Patent No. 7494982. Withdrawal of this rejection is respectfully requested.

Applicants believe that the application is in condition for allowance. If the Examiner

believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-566-7106.

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Respectfully submitted,

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